Notice of Allowability	Application No.	Applicant(s)	
	09/635,679	HABENER, JOEL F.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *11/24/03, 2/19/04 and 2/23/04*.

2. ☒ The allowed claim(s) is/are *15-28 and 30-41; now renumbered 1-26 respectively*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☒ to Paper No./Mail Date *21*.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *2/19/04* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

N. M. Minnifield
Primary Examiner
Art Unit: 1645

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Aaron L. Schwartz, 48181 on February 19, 2004.

2. Applicants' amendment filed November 24, 2003 is acknowledged and has been entered. Claims 1-14 and 29 have been canceled. New claims 30-41 have been added. Claims 15-28 and 30-41 are now pending in the present application. All rejections have been withdrawn in view of Applicants' comments filed November 24, 2003.

3. The terminal disclaimer filed on November 24, 2003 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of 5,120,712 has been reviewed and is accepted. The terminal disclaimer has been recorded.

4. The application has been amended as follows:

The previous continuing data on page 1 of the specification has been deleted and the following has been inserted:

--This application is a continuation of U.S. Application No. 09/090,949, filed June 5, 1998, Pat. No. U.S. 6,162,907, which is a continuation of U.S.

Application No. 08/749,762, filed November 20, 1996, Pat. No. U.S. 5,958,909, which is a continuation of U.S. Application No. 08/156,800, filed November 23, 1993, Pat. No. U.S 5,614,492, which is a continuation of U.S. Application No. 07/756,215, filed September 5, 1991, abandoned, which is a continuation-in-part of United States Patent Application No. 07/532,111, filed June 1, 1990, Pat. No. U.S. 5,118,666, which is a file wrapper continuation of U.S. Application No. 07/148,517, filed January 26, 1988, abandoned, which is a continuation-in-part of U.S. Application No. 06/859,928, filed on May 5, 1986 and now abandoned.--

1-14 (Cancelled).

15. (Previously presented) A derivative of glucagon-like peptide-1 (7-37), (GLP-I (7-37)), wherein the amino acid sequence of said derivative has the same number of amino acids as said GLP-I (7-37), and at least 80% amino acid identity to said GLP-I (7-37), and wherein said derivative has an insulinotropic activity that exceeds the insulinotropic activity of GLP-I (1-37) and GLP-I (1-36).

16. (Previously presented) The derivative of claim 15, wherein said derivative has at least 90% amino acid identity to said GLP-I (7-37).

17. (Previously presented) The derivative of claim 15, wherein said derivative has at least 95% amino acid identity to said GLP-I (7-37).

18. (Previously presented) A derivative of glucagon-like peptide-1 (7-37),

(GLP-I (7-37)), wherein the amino acid sequence of said derivative has the same number of amino acids as said GLP-I (7-37), and an insulinotropic activity that exceeds the insulinotropic activity of GLP-I (1-37) and GLP-I (1-36), and wherein the amino acid sequence of said derivative is that of GLP-I (7-37) except that an amino acid residue has been substituted with a different amino acid residue.

19. (Previously presented) The derivative of claim 18, wherein a hydrophobic amino acid residue of GLP-I (7-37) has been substituted with a different hydrophobic amino acid residue.

20. (Previously presented) The derivative of claim 18, wherein a basic amino acid residue of GLP-1 (7-37) has been substituted with a different basic amino acid residue.

21. (Previously presented) The derivative of claim 18, wherein an aromatic amino acid residue of GLP-1 (7-37) has been substituted with a different aromatic amino acid residue.

22. (Currently Amended) ~~A derivative of glucagon-like peptide-1 (7-37), (GLP-1 (7-37))~~ The derivative of claim 15, said derivative having the formula:

(1) H_2N-X-CO-R^1

- wherein R^1 is OH, OM, or -N R^2 R^3;
- M is a pharmaceutically acceptable cation or a lower branched or unbranched alkyl group;

- R^2 and R^3 are the same or different and selected from the group consisting of hydrogen and a lower branched or unbranched alkyl group;

- X is a derivative of glucagon-like peptide-1 (7-37), (GLP-1 (7-37)), wherein the amino acid sequence of said derivative has the same number of amino acids as said GLP-1 (7-37), and has at least 80% amino acid identity to said GLP-1 (7-37);

- NH_2 is the amine group of the amino terminus of X;

- CO is the carbonyl group of the carboxy terminus of X;

(2) the acid addition salts of (1);

(3) the amino or carboxyl protected form of (1);

(4) a pharmaceutically acceptable carboxylate salt of said peptide;

(5) a pharmaceutically acceptable lower alkyl ester of said peptide; or

(6) a pharmaceutically acceptable amide of said peptide;

wherein said derivative has an insulinotropic activity that exceeds the insulinotropic activity of GLP-1 (1-37) and GLP-1 (1-36).

23. (Previously presented) The derivative of claim 22, wherein said derivative has at least 90% amino acid identity to said GLP-1 (7-37).

24. (Previously presented) The derivative of claim 22, wherein said derivative has at least 95% amino acid identity to said GLP-1 (7-37).

25. (Currently Amended) ~~A derivative of glucagon-like peptide-1 (7-37), (GLP-1 (7-37))~~ The derivative of claim 18, said derivative having the formula:

(1) H_2N-X-CO-R^1

- wherein R^1 is OH, OM, or -N R^2 R^3;
- M is a pharmaceutically acceptable cation or a lower branched or unbranched alkyl group;
- R^2 and R^3 are the same or different and selected from the group consisting of hydrogen and a lower branched or unbranched alkyl group;
- X is a derivative of glucagon-like peptide-1 (7-37), (GLP-1 (7-37)), wherein the amino acid sequence of said derivative is that of GLP-1 (7-37) except that an amino acid residue has been substituted with a different amino acid residue;
- NH_2 is the amine group of the amino terminus of X;
- CO is the carbonyl group of the carboxy terminus of X;

(2) the acid addition salts of (1);

(3) the amino or carboxyl protected form of (1);

(4) a pharmaceutically acceptable carboxylate salt of said peptide;

(5) a pharmaceutically acceptable lower alkyl ester of said peptide; or

(6) a pharmaceutically acceptable amide of said peptide;

wherein said derivative has an insulinotropic activity that exceeds the insulinotropic activity of GLP-1 (1-37) and GLP-1 (1-36).

26. (Previously presented) The derivative of claim 25, wherein a hydrophobic amino acid residue of GLP-1 (7-37) has been substituted with a different hydrophobic amino acid residue.

27. (Previously presented) The derivative of claim 25, wherein a basic amino acid residue of GLP-1 (7-37) has been substituted with a different basic amino acid residue.

28. (Previously presented) The derivative of claim 25, wherein an aromatic amino acid residue of GLP-1 (7-37) has been substituted with a different aromatic amino acid residue.

29. (Canceled).

30. (Previously presented) A compound which is:

(A) a peptide having at least 80% homology with glucagon-like peptide-1 (7-37) (GLP-I (7-37)), with the proviso that the peptide is not GLP-I (7-34),

GLP-I (7-35), GLP-I (7-36) or GLP-I (7-37); or

(B) a peptide which is

(i) a pharmaceutically acceptable acid addition salt of (A);

(ii) a pharmaceutically acceptable carboxylate salt of (A);

(iii) a pharmaceutically acceptable lower alkyl ester of (A); or

(iv) a pharmaceutically acceptable amide, alkyl amide or dialkyl amide of (i), (ii), or (iii);

wherein the compound is substantially free of natural contaminants, and has an insulinotropic activity which exceeds the insulinotropic activity of GLP-I (1-36) or GLP-1 (1-37).

31. (Previously presented) A compound according to claim 30 having an insulinotropic activity at a concentration of at least 10^{-11} M.

32. (Previously presented) A compound according to claim 30, having an insulinotropic activity at a concentration of at least10^{-10} M.

33. (Currently Amended) An insulinotropic medicament comprising an insulinotropically effective amount of a compound according to claim 30 in combination with a pharmaceutically acceptable carrier.

34. (Previously presented) A compound which is:

(A) a peptide having at least 80% homology with glucagon-like peptide-l (7-36) (GLP-I (7-36)), with the proviso that the peptide is not GLP-I (7-34), GLP-I (7-35), GLP-I (7-36) or GLP-I (7-37); or

(B) a peptide which is

(i) a pharmaceutically acceptable acid addition salt of (A);

(ii) a pharmaceutically acceptable carboxylate salt of (A);

(iii) a pharmaceutically acceptable lower alkyl ester of (A); or

(iv) a pharmaceutically acceptable amide, alkyl amide or dialkyl amide of (i), (ii), or (iii);

wherein the compound is substantially free of natural contaminants, and has an insulinotropic activity which exceeds the insulinotropic activity of GLP-I (1-36) or GLP-1 (1-37).

35. (Previously presented) A compound according to claim 34 having an insulinotropic activity at a concentration of at least 10^{-11} M.

36. (Previously presented) A compound according to claim 34, having an insulinotropic activity at a concentration of at least 10^{-10} M.

37. (Currently Amended) An insulinotropic medicament comprising an insulinotropically effective amount of a compound according to claim 34 in combination with a pharmaceutically acceptable carrier.

38. (Previously presented) A compound which is:

(A) a peptide having at least 80% homology with glucagon-like peptide-l (7-35) (GLP- 1 (7-35)) or glucagon-like peptide-l (7-34) (GLP-I (7-34), with the proviso that the peptide is not GLP-I (7-34), GLP-I (7-35), GLP-I (7-36) or GLP-I (7-37); or

(B) a peptide which is

(i) a pharmaceutically acceptable acid addition salt of (A);

(ii) a pharmaceutically acceptable carboxylate salt of (A);

(iii) a pharmaceutically acceptable lower alkyl ester of (A); or

(iv) a pharmaceutically acceptable amide, alkyl amide or dialkyl amide of (i), (ii), or (iii);

wherein the compound is substantially free of natural contaminants, and has an insulinotropic activity which exceeds the insulinotropic activity of GLP-I (1-36) or GLP-1 (1-37).

39. (Previously presented) A compound according to claim 38 having an insulinotropic activity at a concentration of at least 10^{-11} M.

40. (Previously presented) A compound according to claim 38, having an insulinotropic activity at a concentration of at least 10^{-10} M.

41. (Currently Amended) An insulinotropic medicament comprising an insulinotropically effective amount of a compound according to claim 38 in combination with a pharmaceutically acceptable carrier.

5. Claims 15-28 and 30-41 have been allowed and renumbered 1-26 respectively.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is

571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
February 23, 2004

CLEAN COPY OF SPECIFICATION CHANGES

Specification Page 1, Line 1:

This application is a continuation of U.S. Application No. 09/090,949, filed June 5, 1998, Pat. No. U.S. 6,162,907, which is a continuation of U.S. Application No. 08/749,762, filed November 20, 1996, Pat. No. U.S. 5,958,909, which is a continuation of U.S. Application No. 08/156,800, filed November 23, 1993, Pat. No. U.S 5,614,492, which is a continuation of U.S. Application No. 07/756,215, filed September 5, 1991, abandoned, which is a continuation-in-part of United States Patent Application No. 07/532,111, filed June 1, 1990, Pat. No. U.S. 5,118,666, which is a file wrapper continuation of U.S. Application No. 07/148,517, filed January 26, 1988, abandoned, which is a continuation-in-part of U.S. Application No. 06/859,928, filed on May 5, 1986 and now abandoned.

CLEAN COPY OF ALLOWED CLAIMS

15. A derivative of glucagon-like peptide-1 (7-37), (GLP-I (7-37)), wherein the amino acid sequence of said derivative has the same number of amino acids as said GLP-I (7-37), and at least 80% amino acid identity to said GLP-I (7-37), and wherein said derivative has an insulinotropic activity that exceeds the insulinotropic activity of GLP-I (1-37) and GLP-I (1-36).

16. The derivative of claim 15, wherein said derivative has at least 90% amino acid identity to said GLP-I (7-37).

17 The derivative of claim 15, wherein said derivative has at least 95% amino acid identity to said GLP-I (7-37).

18. A derivative of glucagon-like peptide-1 (7-37), (GLP-I (7-37)), wherein the amino acid sequence of said derivative has the same number of amino acids as said GLP-I (7-37), and an insulinotropic activity that exceeds the insulinotropic activity of GLP-I (1-37) and GLP-I (1-36), and wherein the amino acid sequence of said derivative is that of GLP-I (7-37) except that an amino acid residue has been substituted with a different amino acid residue.

19. The derivative of claim 18, wherein a hydrophobic amino acid residue of GLP-I (7-37) has been substituted with a different hydrophobic amino acid residue.

20. The derivative of claim 18, wherein a basic amino acid residue of GLP-1 (7-37) has been substituted with a different basic amino acid residue.

21. The derivative of claim 18, wherein an aromatic amino acid residue of GLP-1 (7-37) has been substituted with a different aromatic amino acid residue.

22. The derivative of claim 15, said derivative having the formula:

(1) H_2N-X-CO-R^1

- wherein R^1 is OH, OM, or -N R^2 R^3;

- M is a pharmaceutically acceptable cation or a lower branched or unbranched alkyl group;

- R^2 and R^3 are the same or different and selected from the group consisting of hydrogen and a lower branched or unbranched alkyl group;

- X is a derivative of glucagon-like peptide-1 (7-37), (GLP-1 (7-37)), wherein the amino acid sequence of said derivative has the same number of amino acids as said GLP-1 (7-37), and has at least 80% amino acid identity to said GLP-1 (7-37);

- NH_2 is the amine group of the amino terminus of X;

- CO is the carbonyl group of the carboxy terminus of X;

(2) the acid addition salts of (1);

(3) the amino or carboxyl protected form of (1);

(4) a pharmaceutically acceptable carboxylate salt of said peptide;

(5) a pharmaceutically acceptable lower alkyl ester of said peptide; or

(6) a pharmaceutically acceptable amide of said peptide;

wherein said derivative has an insulinotropic activity that exceeds the insulinotropic activity of GLP-1 (1-37) and GLP-1 (1-36).

23. The derivative of claim 22, wherein said derivative has at least 90% amino acid identity to said GLP-1 (7-37).

24. The derivative of claim 22, wherein said derivative has at least 95% amino acid identity to said GLP-1 (7-37).

25. The derivative of claim 18, said derivative having the formula:

(1) H_2N-X-CO-R^1

- wherein R^1 is OH, OM, or -N R^2 R^3;
- M is a pharmaceutically acceptable cation or a lower branched or unbranched alkyl group;
- R^2 and R^3 are the same or different and selected from the group consisting of hydrogen and a lower branched or unbranched alkyl group;

- X is a derivative of glucagon-like peptide-1 (7-37), (GLP-1 (7-37)), wherein the amino acid sequence of said derivative is that of GLP-1 (7-37) except that an amino acid residue has been substituted with a different amino acid residue;

- NH_2 is the amine group of the amino terminus of X;

- CO is the carbonyl group of the carboxy terminus of X;

(2) the acid addition salts of (1);

(3) the amino or carboxyl protected form of (1);

(4) a pharmaceutically acceptable carboxylate salt of said peptide;

(5) a pharmaceutically acceptable lower alkyl ester of said peptide; or

(6) a pharmaceutically acceptable amide of said peptide;

wherein said derivative has an insulinotropic activity that exceeds the insulinotropic activity of GLP-1 (1-37) and GLP-1 (1-36).

26. The derivative of claim 25, wherein a hydrophobic amino acid residue of GLP-1 (7-37) has been substituted with a different hydrophobic amino acid residue.

27. The derivative of claim 25, wherein a basic amino acid residue of GLP-1 (7-37) has been substituted with a different basic amino acid residue.

28. The derivative of claim 25, wherein an aromatic amino acid residue of GLP-1 (7-37) has been substituted with a different aromatic amino acid residue.

30. A compound which is:

(A) a peptide having at least 80% homology with glucagon-like peptide-l (7-37) (GLP-I (7-37)), with the proviso that the peptide is not GLP-I (7-34), GLP-I (7-35), GLP-I (7-36) or GLP-I (7-37); or

(B) a peptide which is

(i) a pharmaceutically acceptable acid addition salt of (A);

(ii) a pharmaceutically acceptable carboxylate salt of (A);

(iii) a pharmaceutically acceptable lower alkyl ester of (A); or

(iv) a pharmaceutically acceptable amide, alkyl amide or dialkyl amide of (i), (ii), or (iii);

wherein the compound is substantially free of natural contaminants, and has an insulinotropic activity which exceeds the insulinotropic activity of GLP-I (1-36) or GLP-1 (1-37).

31. A compound according to claim 30 having an insulinotropic activity at a concentration of at least 10^{-11} M.

32. A compound according to claim 30, having an insulinotropic activity at a concentration of at least10^{-10} M.

33. An insulinotropic medicament comprising an insulinotropically effective amount of a compound according to claim 30 in combination with a pharmaceutically acceptable carrier.

34. A compound which is:

(A) a peptide having at least 80% homology with glucagon-like peptide-1 (7-36) (GLP-I (7-36)), with the proviso that the peptide is not GLP-I (7-34), GLP-I (7-35), GLP-I (7-36) or GLP-I (7-37); or

(B) a peptide which is

(i) a pharmaceutically acceptable acid addition salt of (A);

(ii) a pharmaceutically acceptable carboxylate salt of (A);

(iii) a pharmaceutically acceptable lower alkyl ester of (A); or

(iv) a pharmaceutically acceptable amide, alkyl amide or dialkyl amide of (i), (ii), or (iii);

wherein the compound is substantially free of natural contaminants, and has an insulinotropic activity which exceeds the insulinotropic activity of GLP-I (1-36) or GLP-1 (1-37).

35. A compound according to claim 34 having an insulinotropic activity at a concentration of at least 10^{-11} M.

36. A compound according to claim 34, having an insulinotropic activity at a concentration of at least 10^{-10} M.

37. An insulinotropic medicament comprising an insulinotropically effective amount of a compound according to claim 34 in combination with a pharmaceutically acceptable carrier.

38. A compound which is:

(A) a peptide having at least 80% homology with glucagon-like peptide-1 (7-35) (GLP- 1 (7-35)) or glucagon-like peptide-1 (7-34) (GLP-I (7-34), with the proviso that the peptide is not GLP-I (7-34), GLP-I (7-35), GLP-I (7-36) or GLP-I (7-37); or

(B) a peptide which is

(i) a pharmaceutically acceptable acid addition salt of (A);

(ii) a pharmaceutically acceptable carboxylate salt of (A);

(iii) a pharmaceutically acceptable lower alkyl ester of (A); or

(iv) a pharmaceutically acceptable amide, alkyl amide or dialkyl amide of (i), (ii), or (iii);

wherein the compound is substantially free of natural contaminants, and has an insulinotropic activity which exceeds the insulinotropic activity of GLP-I (1-36) or GLP-1 (1-37).

39. A compound according to claim 38 having an insulinotropic activity at a concentration of at least 10^{-11} M.

40. A compound according to claim 38, having an insulinotropic activity at a concentration of at least 10^{-10} M.

41. An insulinotropic medicament comprising an insulinotropically effective amount of a compound according to claim 38 in combination with a pharmaceutically acceptable carrier.